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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b., Unit II B.2.a. (human effects) and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
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1/26/93

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).

o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.

othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.

othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

CAS # Not known
Chem: Lead chromate paints
Title: An epidemiological study of lead chromate paints: Final Report
Date: July 1976
Summary of Effects: Study states 'the study strongly suggested but did not demonstrate unequivocally that male populations exposed to lead chromate inconcentrations often exceeding currently acceptable time weighted averages, have an excess of lung cancer'. However, this conclusion is not supported by the study and the study is therefore insufficient from which to reliably ascribe an effect or a causal relationship to a chemical since:

1) there are no tables from which to determine whether there are any stastically significant excesses;
2) almost no observed or expected numbers are given in the text;
3) no standardized mortality ratios are given in the text;

AN EPIDEMIOLOGICAL STUDY OF LEAD CHROMATE PLANTS: "FINAL REPORT"

Prepared for

The Dry Color Manufacturers Association

Prepared by

Equitable Environmental Health, Inc.
2180 Milvia Street
Berkeley, California 94704

July 1976

A Subsidiary of The Equitable Life Assurance Society of the United States

AN EPIDEMIOLOGICAL STUDY OF LEAD CHROMATE PLANTS

Final Report
July 1, 1976

Submitted to

The Dry Color Manufacturers Association

By

Equitable Environmental Health, Inc.
2180 Milvia Street
Berkeley, California 94704

In July 1974, Tabershaw/Cooper Associates, Inc., now Equitable Environmental Health, Inc., received a request from the Dry Color Manufacturers Association (DCMA) to submit a proposal for an epidemiological study of lead chromate plants. This was to be in two parts: analysis of mortality and estimation of current and past exposures. Such a proposal was submitted on August 21, 1974; an agreement was reached; and operations began in November 1974.

The background of the study is described in the full reports. It arose out of the unresolved question as to whether lead chromate, which is relatively insoluble, shares the carcinogenic potential of more soluble hexavalent chromium compounds.

The present report is in two parts, which were submitted independently. The first describes the mortality analyses, the second the results of industrial hygiene surveys. These were carried out in the same three plants, located in West Virginia, New Jersey, and Kentucky. One began

operation in the mid-1920s, one in 1941, and one in 1949.

The study of mortality was under the direction of William R. Gaffey, Ph.D. A population of 577 male workers, who had been exposed to lead chromate for at least 6 months at some time before December 1974, was identified. The vital status of 548 (95 percent) was determined as of December 31, 1974. There were 53 deaths; 50 death certificates were obtained.

A preliminary report of proportionate mortality in mid-1975, at a time when 38 death certificates had been received, showed 28.9 percent to have been from lung cancer. At this time, the DCMA was advised, and they in turn notified the National Institute for Occupational Safety and Health (NIOSH) on October 2, 1975.

Final analysis of mortality in the population showed 10 of the 50 certified deaths to have been from lung cancer, bringing the proportionate mortality from that cause to 20 percent.

More sophisticated analysis is presented in the enclosed report. It is complicated by the fact that in one of the three plants there was a unit, through which most of the work force rotated, where zinc chromate was produced about one-fourth of the time. Because of the mixed exposure, the population from this plant was analyzed separately.

The small number of deaths from major causes made tests for statistical significance unjustifiable. Nevertheless, there appeared to be an excess of respiratory cancer in the workers studied, the excess generally occurring in older long-term workers. When men with mixed

exposures are excluded, the excess is based on only three deaths, however, so the relative amount cannot be determined precisely. The findings are consistent with the hypothesis that lead chromate is a respiratory carcinogen, but do not justify any other conclusion. Clearly the continued study of this population and of other populations exposed to lead or zinc chromate is warranted.

The occurrence of five cases of stomach cancer in one of the plants, nearly eight times the number expected, was a finding that necessitates more detailed investigation.

The industrial hygiene study was carried out by Mr. Charles D. Yaffe and Mrs. Barbara Kawahara; the plants were visited between January 15 and March 13, 1975. Measurements of airborne lead and chromium showed that for the three plants combined, time-weighted average concentrations at the breathing-zone level reached or exceeded current OSHA standards in nearly one-half of the samples. All plant averages exceeded both current and proposed OSHA standards for lead, and greatly exceeded NIOSH-proposed standards for noncarcinogenic and carcinogenic chromium (VI).

Based on changes in operating methods, equipment, and ventilation, past exposures to lead and chromium were probably more severe than at present in all three plants. Changes in sampling and analytic procedures, however, made it impractical to quantitate such trends.

In summary, the study strongly suggested, but did not demonstrate unequivocally, that male populations occupationally exposed to lead chromate in concentrations often exceeding currently acceptable time-weighted

averages, have an excess of lung cancer. The small number of deaths that occurred in the populations, and the presence of mixed exposure to zinc chromate in one plant, made a definitive conclusion impossible. The result was consistent with the earlier report of an excess in proportionate mortality from lung cancer in the same population.

The staff of Equitable Environmental Health, Inc. wishes to thank those in the participating plants who provided ready access to information in both phases of the study. It also expresses its appreciation to members of the Lead Chromate Sub-committee of the Dry Color Manufacturers Association who assisted in making administrative arrangements, provided valuable technical information on industrial processes, and pushed constantly for completion of the study and presentation of conclusions.

W. Clark Cooper, M.D.
July 1, 1976

A MORTALITY STUDY OF WORKERS IN LEAD CHROMATE PLANTS

Final Report
July 1, 1976

Submitted to

The Dry Color Manufacturers Association

By

Equitable Environmental Health, Inc.
2180 Milvia Street
Berkeley, California 94704

I. INTRODUCTION AND BACKGROUND

In November 1974, Equitable Environmental Health, Inc. (EEH) began, under contract with the Dry Color Manufacturers Association, an evaluation of the health of workers involved in the production of lead chromate. The evaluation took the form of an industrial hygiene survey and a historical prospective mortality study of exposed workers. This report is concerned with the mortality study.

It has long been known that workers exposed in the past to the chromium compounds encountered in basic chromate production facilities have had an increased risk of respiratory cancer (1), although with later reductions in exposure levels this increase may have diminished or disappeared. Nevertheless, the appearance of the increased respiratory cancer mortality gave rise to concern about the extent to which a similar hazard might be present in other chromate compounds, including those used in the production of pigments. In 1975, a Norwegian study of pigment workers exposed to zinc chromate found an excess lung cancer

mortality stated to be about 40 times the expected figure. Although the finding was based on only three deaths, it gave rise to further general concern about the chromates used in pigment production (2).

The present study examined all causes of death, although initially the greatest concern was respiratory cancer in relation to unequivocal exposure to lead chromate in the absence of other possible carcinogens. For reasons that will be explained in Section IV, it was not possible to obtain such a clear-cut relationship in all the plants studied, and the results must be interpreted with that fact in mind.

II. STUDY DESIGN

A population of workers who had been exposed to lead chromate for at least 6 months at some time before December 1974 was identified from personnel records in three plants. Those who had left employment before the study was begun were traced through the Social Security Administration, and death certificates were obtained for those found to have died. Cause of death was determined from the death certificates using the WHO criteria, which are used as the basis for published vital statistics.

Using the ages and lengths of time of observation of each study member, a calculation was made of the number of deaths that would have been expected if the study population had had, at each age and for each cause, the same mortality rates as the male population of the state in which each plant was located. The observed deaths, by cause, were then expressed as a percentage of the expected deaths. The 1960 male

population of the state in which each plant was located was used as a standard for comparison. In addition, for respiratory cancer and stomach cancer, other local and national mortality rates were also used. The rationale and a detailed explanation of the procedure are given in Sections VIII and IX.

III. DATA COLLECTION AND FOLLOW-UP

Plant 1. This plant began operations with lead chromate in 1949, and had 158 employees in exposed jobs at the time of the study. Plant management provided a list of all employees (247 men), past and present, who had worked in exposed jobs. Those whose current vital status was unknown (90 men) were traced through the Social Security Administration. Since the exposed employees in Plant 1 were a small part of the total work force, they had to be identified by a tedious and time-consuming review of all present and past work histories. In order to verify the completeness of the list provided by the plant, EEH representatives took a random sample of plant records, identified exposed workers in the sample, and checked to see if they had indeed been included in the list provided by the plant. No discrepancies were found. Table 1 shows the final results of follow-up.

Plant 2. This plant, with 104 employees currently working in exposed jobs, began operations in the 1920s. Complete employee records were available back to 1959. Management provided a list of 166 present and past employees with at least 6 months' exposure. A total

of 62 names were sent to Social Security for follow-up. Table 1 shows the distribution by vital status of the men from Plant 2 after completion of follow-up.

Plant 3. This plant was the oldest of the three plants. It began lead chromate operations in 1941. Management had reconstructed a list of employees on the wage roll as of June 30, 1957, from which the study population of Plant 3 was selected. The work records of the cohort both before and after the 1957 date were reviewed, and 164 exposed employees were identified. The names of 128 of these were submitted to Social Security. The follow-up is shown in Table 1.

The subsequent analysis is concerned with the 548 men whose vital status is known, i.e., 238, 152, and 158 from Plants 1, 2, and 3.

Overall, 94.97 percent of the study population was successfully traced, the percent ranging from 91.57 in Plant 2 to 96.36 percent in Plant 1. A total of 53 deaths were found, and death certificates were obtained for 50 of these.

At first glance, the large percentage of deaths in Plant 3 may appear surprising. However, all of the Plant 3 population had been rehired before 1957, while the other two plant populations included recent hires who were younger, and therefore less likely to have died.

IV. EXPOSURE AND DURATION OF EMPLOYMENT

Plants 1 and 2 had well-defined lead chromate operations with no opportunities for exposure to other chromate products. However, the industrial hygiene survey of Plant 3 revealed that one of the lead

chromate production units in that plant spent 2 weeks out of every 8 in the production of zinc chromate, and that this unit had been in operation since 1947. Individuals who worked in this unit, therefore, had a mixed exposure. Further, since men were rotated through different units as a result of promotions or reductions in force, it was clear that an indeterminate number of men employed in other units of the plant with pure lead chromate exposure might in the past have had some zinc chromate exposure.

In order to clarify the situation, a list of all job titles found in all of the work histories from Plant 3 was compiled and sent back to the plant. Plant management was asked to characterize the exposure in each job as lead chromate only, zinc chromate only, both, or neither, and to do this by time period if the exposures had changed as a result of process changes. The job history of each study member from Plant 3 was then computerized, entering for each job the kind of exposure involved.

Analysis revealed that there were two men in the Plant 3 group whose entire exposure had been to lead chromate alone, and none whose entire exposure had been to zinc chromate alone. Of the former two men, one was not included in the study analysis because he was among the men who could not be traced, and the other died of lung cancer.

As a result of the mixed exposure in Plant 3, data from that plant were analyzed separately from the data from Plants 1 and 2.

In the subsequent sections, the most meaningful tables deal with men hired before 1960 who were employed for more than 10 years. Be-

cause of past patterns of hiring and of movement among different jobs, duration of employment may not be the same as duration of exposed employment. To the extent that this is true, the mortality ratios presented are slightly lower than they would have been if it had been possible to modify the computer programs to take account only of exposed employment.

V. ANALYSIS - GENERAL

In a preliminary report prepared by EEH, about midway in the study, the mortality data then available were presented as a proportional mortality analysis, i.e., respiratory cancer deaths were expressed as a percentage of all deaths found at that time, the percent being 28.9 for the total study group. The percentage for the total group is now 20.0, but the analysis will not be pursued in the present report. The reason is that a proportional mortality analysis is an expedient, which is useful when a complete follow-up is not available, but which does not give actual risk figures as does the analysis described in Section II.

Tables 2 and 3 show Standardized Mortality Ratios (SMRs) (i.e., observed deaths as a percent of expected deaths) for selected causes in Plants 1 and 2 in the first table and in Plant 3 in the second. Where appropriate, the cause-specific SMRs have been corrected to account for deaths from unknown causes, that is, for which death certificates could not be found, assuming that the missing certificates would have the same cause distribution as those that had been obtained. For example,

in Table 2 there are 14 deaths in Plant 1, for two of which certificates could not be obtained. The observed number of deaths from each known cause was therefore increased by 2/12 to correct for the two missing certificates.

Overall, every plant had fewer deaths than expected, a finding that for several reasons, is not surprising in an employed population. The SMR from malignancies, however, was higher than the overall SMR. In the case of Plants 1 and 2, this was due entirely to respiratory cancer. In Plant 3, in addition, there were excess deaths from digestive cancers. Ulcers of the stomach and cirrhosis of the liver showed excess mortality in some of the plants, but the ratios are based on only one case in each instance.

As is apparent from the descriptions in Section III of how the populations were selected, the populations from Plants 1 and 2 are diluted with recent hires and short-term employees. This has two consequences. First, deaths in the recent hires from respiratory cancer, or any other chronic condition that involves a latent period, cannot legitimately be attributed to this occupational exposure. In fact, one of the respiratory cancer deaths in Plant 2 (who died early in his employment) showed X-ray evidence suggestive of lung cancer before coming to work at the plant. Second, the risk of death in young, recently hired men will, in general, be much less than expected, because this group has been selected for good health through preemployment examinations and through self-selection. As a result, an excess mortality

in older long-term workers may be outweighed by low rates in the younger men, thus concealing, or at least reducing, the apparent risk from occupationally related causes.

Section VI addresses this problem by examining appropriate subgroups of the study population.

VI. ANALYSIS - HIRE DATE AND LENGTH OF EMPLOYMENT

Out of the study population in the first two plants, 181 men from Plant 1 and 45 men from Plant 2 were hired before 1960, and therefore had a minimum latent period of 15 years as of the end of 1974. Table 4 shows SMRs by cause for these two groups.

The major difference between Table 4 and Table 2, which shows data for the total study group in Plants 1 and 2, is in the SMR for respiratory cancer in Plant 2, which is zero for those hired before 1960. The two respiratory cancer cases in Plant 2 were hired after 1960 and died less than 2 years after they were hired, so that their deaths are extremely unlikely to have arisen from exposures during their employment.

In order further to identify those men who had both a long latent period and a long exposure, Table 5 shows, for men hired before 1960, the distribution by duration of employment. Of the pre-1960 hires, there were 37 and 22 men with 10 years or more employment in Plants 1 and 2, and 138 such men in Plant 3. Table 6 shows SMRs for those in Plants 1 and 2, and Table 7 shows SMRs for those in Plant 3.

Plant 1 shows a sharply increased SMR from lung cancer, while Plant 3 shows an increased SMR from respiratory cancer, and a somewhat smaller increase in digestive cancer. Plant 2 has no cancer of any site in this group.

In summary, all plants show excess mortality from respiratory cancer. In Plants 1 and 3 it occurs in the older, long-term employees, while in Plant 2 it occurs in employees whose length of service makes it unlikely that the cancers were occupational in origin.

In Plant 3, an excess of digestive cancer occurs, and is concentrated in workers with 10 years or more service. Of the six deaths, five are from stomach cancer, a condition that accounts for about 27 percent of digestive cancer deaths in the general population.

VII. ANALYSIS - PURE LEAD CHROMATE EXPOSURE

In Plant 3, there was one study group member with a pure lead chromate exposure, who died of lung cancer. He had been hired before 1960 and had worked for more than 10 years. Strictly speaking, an analysis of mortality in men with a pure lead chromate exposure should include this man with the corresponding groups studied in Plants 1 and 2. Table 8 shows SMRs for this total group of 60 men, which consists of all men, from any of the plants, who had a pure lead chromate exposure, who had been hired before 1960, and who had worked at least 10 years. It includes the single worker from Plant 3, workers from Plant 1, and those in Plant 2 who had no respiratory cancer deaths but were

nevertheless exposed to the risk of death from respiratory cancer. The respiratory cancer SMR, based on three cases, is 350.

VIII. ANALYSIS - STATISTICAL CONSIDERATIONS

A. The Choice of a Comparison Population

Because mortality data are available in considerable detail for the general male population, both nationally and by state, such figures are commonly used to calculate the number of expected deaths in studies such as this one.

One general problem with such calculations is that an employed population, as mentioned in Section V, will ordinarily have a lower mortality than the general population. Preemployment examinations, self-selection, and the effects of physical exercise may all be partly responsible for the generally favorable mortality experience of employed groups. However, this effect is most apparent in mortality from cardiovascular disease, and least apparent in cancer, so that the use of the general population as a standard is less of a problem when cancer mortality is of concern (3).

More important problems, specific to the present study, are regional differences in respiratory cancer mortality and the sharp increase in respiratory cancer mortality over time. The regional differences were dealt with by using the mortality statistics for the state in which each plant was located. Nevertheless, there are con-

siderable differences in respiratory cancer mortality even within a given state. Further, the state data used were for 1960.

Two legitimate questions may therefore be raised. First, if the plants are located in counties with an unusually high respiratory cancer mortality, is it not possible that the apparent "excess" mortality simply reflects the high rate in the county in which each plant is located? Second, since the observed mortality occurred over a period, depending on the plant, from some time in the 1950s to 1974, would it not be more valid to use the average respiratory cancer mortality as a standard, rather than the 1960 data?

Tables 9 and 10 provide information on both these points. For each plant, the following data are presented: first, the state mortality rates for respiratory cancer in 1960 and 1970, and second, the average age-adjusted respiratory cancer rates for the period 1950-1969, for the county in which the plant is located. Table 9 shows the rates for whites and Table 10 for nonwhites (4, 5, 6). Although the county rates are adjusted to the age distribution of the United States population, the effect of the age adjustment is unlikely to be large enough to change the interpretation of the tables. Keeping in mind that respiratory cancer mortality rates were steadily increasing from 1960 to 1970, Table 9 shows that for white males the average county mortality for the counties in question was less than the 1960 state rates for Plants 1 and 3, and somewhat greater for Plant 2. Table 10 shows that nonwhite mortality in the counties was greater than the 1960 state rates in all cases.

For Plant 1, the implication of the tables is that the use of the 1960 state rates may have resulted in an overestimate of the expected respiratory cancer deaths. This is so because the population of the county and the plant work force are overwhelmingly white, and the average county mortality for white males in Table 9 is less than the 1960 state rates.

For Plant 2, the tables show that the choice of the 1960 state rates led to an underestimate of the number of expected respiratory cancer deaths. This underestimate did not affect the SMRs for respiratory cancer in Tables 4 and 6, since they were already zero, but did affect the SMRs for Plants 1 and 2 combined.

In Plant 3, the 1960 state rates apparently overestimated the number of expected deaths for whites but underestimated the number for nonwhites. The net effect therefore depends on the proportion of nonwhites in the Plant 3 cohort.

All of these issues of regional differences and time trends could be resolved if detailed male mortality rates by age, race, and cause were available by county or other local areas for different years. Expected deaths, corrected for local differences and for time trends, could then be obtained. Such data have in fact become available for 1970, but not for 1960. In Section IX, the 1970 county data are used in conjunction with the 1960 state data to recalculate the expected respiratory cancer deaths, with a partial correction for

regional variation and time periods. A similar calculation is performed for stomach cancer mortality.

B. Tests of Statistical Significance

No tests of statistical significance are given for the observed SMRs because the numbers of expected deaths in the categories of interest, lung cancer and, in Plant 3, digestive cancer, are all less than 5. In view of the uncertainties involved in statistical tests with such small numbers, the results would have to be considered equivocal.

IX. CANCER MORTALITY - REGIONAL AND TIME TREND CORRECTIONS

Plant 1. Respiratory cancer mortality rates were obtained for 1970 for all males, by age, for the county in which most of the Plant 1 workers resided. (The rates could not be obtained by race because of the small number of nonwhite.) These rates were applied to that portion of the Plant 1 experience that occurred after the middle of 1965. The resulting expected death calculation is therefore corrected for regional and time trends for that portion of the plant's experience occurring after mid-1965. Table 13 shows the resulting SMR for respiratory cancer in men hired before 1960 who worked 10 years or more. The value is 200.6.

Plant 2. Respiratory cancer mortality in 1970, by age and race, was obtained for males in the Standard Metropolitan Statistical Area (SMSA) within which the plant was located. The expected deaths were calculated on the conservative assumption that one-half of the Plant 2 experience was among nonwhite employees, and are shown in Table 13. For this plant, differences by race were not large. If an all white population had been assumed, the expected value would have been about 12 percent smaller. The SMR, of course, is still zero for Plant 2.

Plant 3. Expected respiratory cancer deaths were calculated in exactly the same way as in Plant 2, using the mortality data for the SMSA of Plant 3. In this case, however, the assumption of a 50 percent nonwhite experience agrees with estimates of the actual percent nonwhite in the cohort. The SMR, shown in Table 14, is 189.3.

A similar analysis was made of stomach cancer mortality in Plant 3, since the digestive cancer that occurred in that plant was predominately stomach cancer. Male stomach cancer mortality by age and race was obtained for the SMSA, in 1970, and stomach cancer mortality by age for all males in the United States was obtained for 1960. (Stomach cancer data by state were not available for 1960.) Table 14 shows the details of the SMR calculation. The value was 778.3.

X. DISCUSSION AND CONCLUSIONS

A. Respiratory Cancer Mortality

Interpretation of the study results is complicated by three problems. The first is that one of the plants had a mixed exposure.

The second is that the number of deaths was small, particularly in the plants with a pure exposure, and particularly from lung cancer. As a result of the second fact, none of the excess mortality was tested for statistical significance, and the excess lung cancer mortality among workers with a pure lead chromate exposure is based on three deaths.

The third problem is that, since only three plants were studied, the observed mortality may be a function of local background mortality, so that state mortality rates may not be an appropriate standard. A partial adjustment for this factor, and for time trends in respiratory cancer mortality, led to a reduction in the excess respiratory cancer mortality. Had a complete analysis using county or regional mortality been possible, the result might have been a further reduction or an increase.

Examination of the lung cancer deaths does little to clarify the situation. An inquiry into the smoking histories of these men was made at the plants where the men were employed. Table 11 lists the deaths, with the relevant facts about age, employment, and smoking history. The last death listed was one known by the plant to have been lung cancer, but was incorrectly attributed to acute hemorrhage and pneumonia on the death certificate. Since the population mortality rates used as a basis for comparison in this study are based only on death certificate information, this death was not counted as lung cancer in the mortality tables, but is included in Table 11 for completeness.

All the men except one were known to be cigarette smokers, although the amount and duration of smoking was unknown in most cases. It did not appear that inquiries to the next of kin would have added anything substantial to the information obtained from the plants.

It is possible that cigarette smoking could account for the excess lung cancer, either by itself or as an agent that interacted with an occupational exposure.

The former hypothesis could be tested by examining mortality among unexposed men in the same plants. Very limited data of this kind were inadvertently obtained during data collection in Plant 3, and presented in the Progress Report, showing one lung cancer death (a smoker) out of 11 deaths in unexposed men. This proportion is about one-third of what was observed in the exposed population, but the number of cases involved is small and confined to workers in Plant 3.

It is possible to hypothesize that the excess lung cancer in Plant 3 was the result of zinc chromate exposure and that the excess in men with a pure lead chromate exposure was due to chance. However, this view attaches very strong significance to the three deaths on which the conclusions of the Norwegian zinc chromate study were based, and no significance at all to the three deaths in Table 8. In fact, although the relative excess represented by the three cases in the zinc chromate study was greater than that represented by the three

"pure" lead chromate cases in the present study, the numbers were small in both studies.

One is left with the fact that there is an excess of respiratory cancer in the workers studied; that the excess generally occurs in older, long-term workers; that the excess, excluding men with mixed exposure, is based on only three deaths; and that the relative amount of the excess cannot be determined precisely. The findings are consistent with the hypothesis that lead chromate is a respiratory carcinogen, but do not justify any further conclusion.

Extensive studies are now being undertaken in Europe and the United Kingdom with large populations of lead, zinc, and other chromate workers. The evidence provided by those studies may clarify the situation.

B. Digestive Cancer Mortality

Table 12 is a list of the deaths from digestive cancer, all of which occurred in Plant 3 among men who had worked 10 years or more. Since the digestive cancer is essentially stomach cancer in these cases, the SMR for digestive cancer in Table 7 understates the relative risk. Table 14 shows the SMR for stomach cancer in Plant 3 to be 778. Although this figure is subject to the same qualifications as the respiratory cancer SMRs, it is so large that its value would not be materially affected by a change in the standard population used.

No digestive cancer was found in the other two plants studied, and there is no mention of stomach cancer as a consequence of chromate exposure in the scientific literature. The 1950-1969 age-adjusted mortality rates for stomach cancer in the county where Plant 3 is located is significantly higher than the national average, but is not among the highest 10 percent of United States rates (5). Racial differences in digestive cancer in the state show about a one-third excess for nonwhites. In any case, the figure of 778 includes at least a partial adjustment for these factors.

Although it is possible, it does not appear likely that the excess is due to either zinc or lead chromate. If the first were true, it would be difficult to explain why no stomach cancer was found in the Norwegian study of zinc chromate workers. If the second were true, one would expect some stomach cancer in Plants 1 and 2. The most likely possibilities appear to be either a common occupational exposure to substances other than chromates, or ethnic and dietary factors. In any case, a thorough investigation of the occupational histories of these men is in order.

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Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12030A

Triage of 8(e) Submissions

Date sent to triage: 12/14/95

NON-CAP (CAP)

Submission number: 12030A

TSCA Inventory: Y N (D)

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

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STOX CTOX (EPI) RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

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Notes:

Contractor reviewer : PMM **Date:** 4/18/95

CECATS/TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-1092-12030 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0570) REFER TO CHEMICAL SCREENING
(0578) CAP NOTICE

VOLUNTARY ACTIONS
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/CUSTOMERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/15/92 OTS DATE: 10/27/92 CSRAD DATE: 01/25/95

CHEMICAL NAME:
Lead chromate Paints
Paint, lead chromate
Chromic acid

CAS#
Unknown none
n/a none
7758-97-6

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
(0216)	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
(0219)	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQ/EST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATE:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	HMN	LOW	paint	
CAS SR	NO	NO (CONTINUE)		MED		
	(IN TERMIN)	REJ-I-R		HIGH		

[illegible]

Tox Concern

ID
12030A

M

COMMENT

EPI: IN 1976 A LARGE INSURER'S SUBSIDIARY THAT CONDUCTS HEALTH STUDIES, COMPLETED AN EPIDEMIOLOGIC STUDY IN THREE PLANTS LOCATED IN WEST VIGINIA, NEW JERSEY AND KENTUCKY. ONLY 50 DEATH CERTIFICATES WERE AVAILABLE FOR ANALYSIS. THE PROPORTION OF DEATHS FROM LUN CANCER WAS 20%, AN APPARENT EXCESS, WHILE 10% DIED OF STOMACH CANCER, AN APPARENT NEARLY 8-FOLD EXCESS. (A 158-WORKER SUB-COHORT OF MOSTLY OLDER TENURED WORKERS IN PLANT 3--WITH ABOUT 25% OF THEIR EXPOSURES TO ZINC CHROMATE--GENERATED 6 DEATHS, 5 FROM STOMACH CANCER). AIRBORNE LEAD AND CHROMIUM MEASUREMENTS REACHED OR EXCEEDED OSHA STANDARDS IN ALMOST HALF OF THE MONITORING SAMPLES. THE SMR FR MEN WITH PURE LEAD CHROMATE EXPOSURE, HIRED BEFORE 1960 WITH AT LEAST 10 YEARS PLANT EMPLYMENT, WAS 350 (3 DEATHS). THE STUDY IS CONSISTENT WITH OTHER FINDINGS THAT SUGEST LEAD CHROMATE IS A RESPIRATORY CARCINOGEN. TOGETHER WITH THEIR INDUSTRIAL HYGIENE SURVEYS (APPARENTLY PUBLISHED SEPARATELY) THESE STUDY DATA MAY HELP TO QUANTIFY RISKS. THIS STUDY PREDATES THE 1984 HAD VUT APPEARS, TOGETHER WITH ITS UPDATE, IN THE 1993 ATSDR CHROMIUM TOXICOLOGIC PROFILE UPDATE.